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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,111	07/23/2001	Hideyuki Matsuda	1581/00265	3002

7590 01/31/2003

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/31/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,111	MATSUDA ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a 371 of application PCT/JP00/05659.

The preliminary amendment filed July 23, 2001 amending claims 4, 7, 8, 9 and 12 and adding claims 13-20 has been entered.

The second preliminary amendment filed April 19, 2002 replacing the Sequence Listing with a substitute Sequence Listing has been entered.

Claims 1-20 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings filed concurrently with the application have been objected by Draftsman, please refer to the attached PTO-948 form for details.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR

1.821 through 1.825. 37 CFR 1.821(d) requires the use of assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences.

The following are examples of incompliance where the sequence containing more than ten nucleotides is given without a sequence identifier: page 5, lines 1 and 2; page 10, lines 17 and 18; page 11, line 11, page 15, lines 6 and 8.

The specification is objected to because of the following.

It refers to the expression vector pUCNT as "(disclosed in WO 94/03613)" (page 15, lines 11-13). This is improper because as an essential material, pUCNT, must be described in the specification.

It appears that Q_{10} is mistyped on page 17, line 16.

There are references to "SEQ ID NO:1 under SEQUENCE LISTING" throughout the specification (e.g., page 10, line 35, emphasis added). The reference to "SEQ ID NO:1" is sufficient.

Claim Objections

Claims 1 and 2 are objected to because of the following informalities:

the conventional way to present a Markush group is "a DNA selected from the group consisting of", for example.

Furthermore, there are no (a), (b), (c) in claim 2 . Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1(b) is directed to a DNA having the sequence obtained by the deletion, addition, insertion and/or substitution of one or a plurality nucleotides of SEQ ID NO:1 wherein said DNA encodes decaprenyl diphosphate synthase activity. Claim 1(c) is directed to a DNA that hybridizes to SEQ ID NO: 1 under undefined stringent conditions wherein said DNA encodes decaprenyl diphosphate synthase activity. Claim 2(e) is directed to a protein having the sequence obtained by the deletion, addition, insertion and/or substitution of one or a plurality of amino acids of SEQ ID NO:2 wherein said protein has decaprenyl diphosphate synthase activity. Claims 3-20 depend from either claim 1 or claim 2. Since number of possible mutations is not limited, this amounts to

any amino acid/nucleotide structure that is not necessarily homologous to SEQ ID NO:1 or SEQ ID NO:2. Thus, the claims are drawn to an enormous genus of a decaprenyl diphosphate synthase both naturally occurring and man made and a DNA encoding thereof.

Applicants disclose a decaprenyl diphosphate synthase from *Saitoella complicata* having the amino acid sequence of SEQ ID NO:2 and a DNA of SEQ ID NO:1 encoding thereof. Therefore, a representative number of species is one. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of being "decaprenyl diphosphate synthase" or a DNA encoding thereof and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-4, 7-10 and 12-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a decaprenyl diphosphate synthase of SEQ ID NO:2 and a DNA encoding thereof, does not reasonably provide enablement for a decaprenyl diphosphate synthase having unknown homology to SEQ ID NO:2 and

a DNA encoding thereof and a DNA having unknown homology to SEQ ID NO:1 and encoding decaprenyl diphosphate synthase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

As discussed above, claims 1 and 2 are directed to a decaprenyl diphosphate synthase of unknown structure and a DNA of unknown structure encoding a decaprenyl diphosphate synthase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of decaprenyl diphosphate synthase enzymes and genes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and

guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of a single decaprenyl diphosphate synthase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass a decaprenyl diphosphate synthase and a DNA encoding thereof with unknown homology to the *Saitoella complicata* decaprenyl diphosphate synthase and a DNA encoding thereof because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting decaprenyl diphosphate synthase activity; (B) the general tolerance of decaprenyl diphosphate synthase to modification and extent of such tolerance; (C) a rational and predictable scheme for

modifying any decaprenyl diphosphate synthase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of modifications in SEQ ID NO:1 and SEQ ID NO:2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claims 5, 6 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and /or use the invention.

Claims 5, 6 and 11 recite pUCNT, pNTSa1 and *E. coli* DH5α (pNTSa1), respectively.

Applicants disclose primers used to obtain pNTSa1 from *Saitoella complicata* IFO 10748 using pUCNT (page 15, lines 1-16). However, it is not apparent whether *Saitoella complicata* IFO 10748 and pUCNT are readily available to the public.

E. coli DH5α (pNTSa1) has been deposited under FERM BP-6844 on August 17 of Heisei 11, 1990 (page 16, lines 8-11). However it is not apparent whether the deposit is readily available to the public. An affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his/her signature, and registration number, stating that the specific plasmids and/or strain(s) has/have been deposited under the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-13, 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a stringent condition". This includes various conditions depending on which different nucleotides will hybridize. Without knowing the exact conditions, it is impossible to know which nucleotides are encompassed by the claim rendering its metes and bounds indefinite.

Claims 4-6 and 13 are confusing as reciting "expression vector" twice. Amending claim 4, for example, to "an expression vector comprising a DNA of claim 1" would obviate this rejection. Also, a DNA is inserted not cloned into the vector.

Claims not specifically discussed herein are rejected as dependent from the rejected claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

A DNA having the sequence of SEQ ID NO:1 and a protein having the sequence of SEQ ID NO:2 are naturally occurring in fungus *Saitoella complicata*. As products of Nature they are unpatentable. Amending the claims the recite "An isolated or purified DNA/protein", for example, would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-9, 12-14 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al.

Suzuki et al. teach a gene (dps) encoding decaprenyl diphosphate synthase from *Schizosaccharomyces pombe*. They teach a vector and an *E. coli* cell comprising thereof. Said cell produces a 378 amino acid long decaprenyl diphosphate synthase having the sequence that is 42% identical to SEQ ID NO:2. Said cell also produces ubiquinone-10 (coenzyme Q_{10}).

Since the number of possible mutations is not limited, decaprenyl diphosphate synthase and gene encoding thereof disclosed by Suzuki et al. anticipate claims 1-3 and the claims dependent thereon.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

January 24, 2003